Electronic Supplementary Material (ESI) for CrystEngComm


*(Supporting Information)*

# The Quest for a Molecular Capsule Assembled *via* Halogen Bonds

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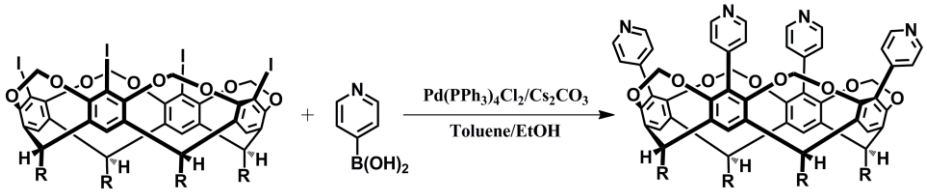
# *Experimental Section*

## *Synthesis*

All chemicals were purchased from Aldrich and Strem chemicals and used without further purification. The determinations of melting points were carried out on Fisher-Johns melting point apparatus and are uncorrected. $^{1}$H NMR and $^{13}$C NMR spectra were recorded on a Varian Unity plus 200 MHz or 400 MHz spectrometer in $CDCl_3$. Compounds were prepared for infrared spectroscopic (IR) analysis as a mixture in KBr.

## *Synthesis of C-pentyltetra(4-pyridyl)cavitand, 1*

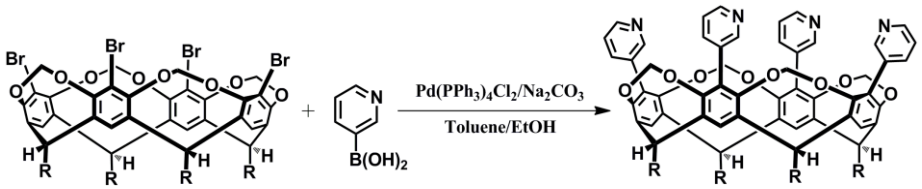



R = $(CH_2)_4CH_3$

**1**

The synthesis follows a slightly modified route from published literature.[1] *C*-Pentyltetraiodocavitand (0.80 g, 0.61 mmol) was placed in a round bottom flask. It was heated to 50 ºC under a stream to dinitrogen for 30 mins with stirring. Toluene (20 mL), ethanol (10 mL) and cesium carbonate (150 mg, 0.46 mmol) were all purged with dinitrogen before being added to the round bottom flask in dinitrogen atmosphere. *Tetrakis*-triphenylphosphine palladium (II) (420 mg, 0.362 mmol) was added to the reaction mixture followed by 4-pyridylboronic acid (0.80 g, 6.52 mmol). The reaction mixture was refluxed at 80 ºC for 72 hours under dinitrogen. Upon completion of the reaction, the mixture was cooled to room temperature and diluted with water (100 mL). The aqueous phase was washed with dichloromethane (3 x 100 mL) and dried with magnesium sulfate. The solvent was removed using rotary evaporator and the residue obtained was purified by column chromatography using ethanol/ethyl acetate/traces of $Et_3N$ mixture as eluant over silica. The product was isolated as a white powder (0.30 g, 45%). M.P. >280 ºC; $^{1}$H NMR (δH; 200 MHz, $CDCl_3$): 8.58 (d, J = 6.0 Hz, 8H), 7.37 (s, 4H), 6.98 (d, J = 6.0 Hz, 8H), 5.29 (d, J = 6.0 Hz, 4H), 4.84 (t, J = 8.0 Hz, 4H), 4.23 (d, 8.0 Hz, 4H), 2.34 (m, 8H), 1.46 (m, 24H), 0.96 (t, J = 7Hz, 12 H); $^{13}$C NMR (δH; 200 MHz, $CDCl_3$): 152.17, 149.46, 142.02, 138.00, 126.83, 124.91, 120.85, 100.39, 43.23, 37.01, 31.99, 30.24, 27.58, 22.68, 14.14. MALDI-TOF / TOF-MS *m/z* 1125 ([**1** + H]$^{+}$).

### *Synthesis of C-pentyltetra(3-pyridyl)cavitand, 2*[1]

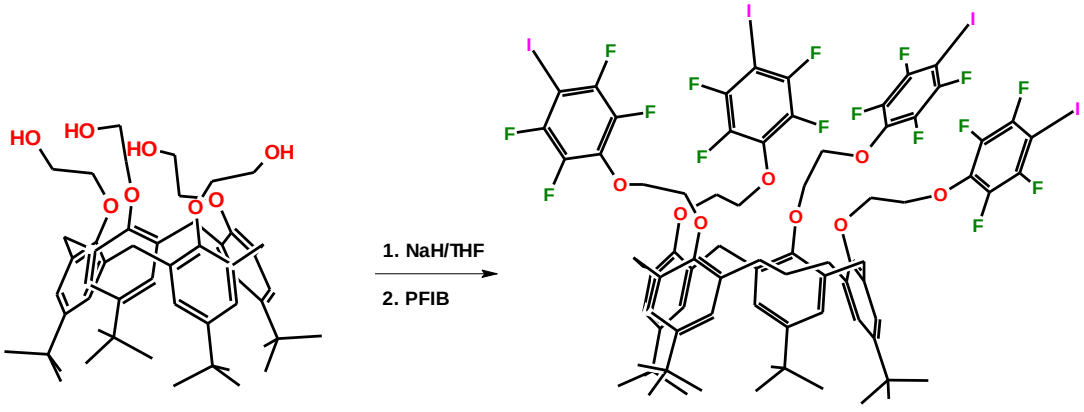



R = $(CH_2)_4CH_3$ **2**

A mixture of C-pentyltetrabromocavitand (2.0 g, 1.77 mmol) and *tetrakis*-triphenylphosphine palladium (II) (420 mg, 0.362 mmol) were added to a round bottom flask under a stream of dinitrogen. Toluene (30 mL), ethanol (20 mL) and aqueous sodium bicarbonate (100 mg, 5 mL) were all purged with dinitrogen before adding to the round bottom flask along with 3-pyridylboronic acid (2.8g, 22.76 mmol). The reaction mixture was refluxed for 72 hours under a dinitrogen atmosphere. Upon completion of the reaction, the mixture was cooled to room temperature and diluted with water (100 mL). The aqueous phase was washed with dichloromethane (3 x 100 mL) and dried with magnesium sulfate. The solvent was removed using rotary evaporator and the residue obtained was purified by column chromatography using ethanol/ethyl acetate mixture as eluant over silica. The product was isolated as a white crystalline solid (1.50 g, 76%). M.P. >280 ºC. $^1$H NMR (δH; 400 MHz, $CDCl_3$): 8.408 (br, 4H), 8.244 (s, 4H), 7.39(s, 8H), 7.183 (br, 4H), 5.243 (br, 4H), 4.881(s, 4H), 4.234 (s, 4H), 2.376 (m, 8H), 1.481 (m, 24H), 0.962 (t, 12H).

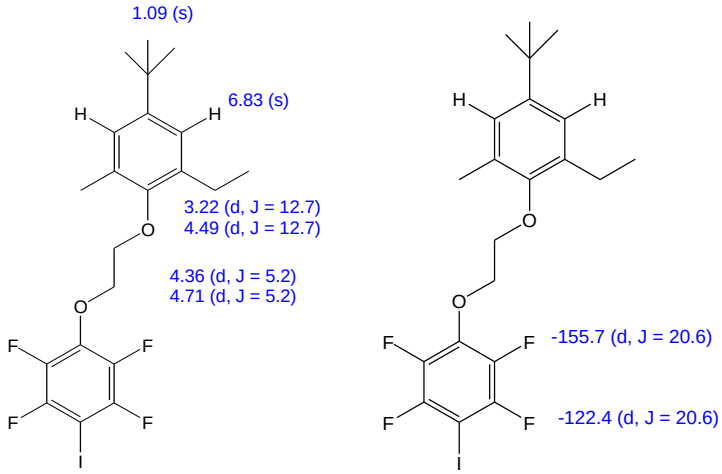
### *Synthesis of tetrakis (hydroxyethyl) ether derivative of p-tert-butylcalix[4]arene, B (in the cone conformation)*[2]

The synthesis of the tetrakis (hydroxyethyl) ether derivative of *p-tert*-butylcalix[4]arene, **B** (in the cone conformation), was obtained using published procedures.




**B**

100 mg (0.121 mmol) of calix and 0.63 mmol of NaH are stirred in 0.3 mL of THF during 40 min. Then, 0.13 mL (0.97 mmol) of PFIB are added and the mixture is refluxed during 24h. After this time, $CH_2Cl_2$ and water are added, the aqueous layer is extracted 3 times with $CH_2Cl_2$ and the organic layer is dried over $Na_2SO_4$. The crude mixture was purified by flash chromatography on silica gel (230-400 mesh) using petroleum ether (b.p. 40 – 60 °C) as eluent to obtain the tetrasubstituted calix in 80 % yield in the form of a microcrystalline white powder (m.p. 114-117 °C).




$^1$H NMR (500 MHz, $CDCl_3$) : δ 6.83 (8H, s, H arom.), 4.71 (8H, d, *J* = 5.2, O-$CH_2$), 4.49 (4H, d, *J* = 12.7, $CH_2$), 4.36 (8H, d, *J* = 5.2, O-$CH_2$) 3.22 (4H, d, *J* = 12.7, $CH_2$) ; $^{19}$F NMR (470 MHz, $CDCl_3$) : δ -155.7 (8F, d, *J* = 20.6, CF-CO), -122.4 (8F, d, *J* = 20.6, CF-CI).

FT-IR (UATR) (selected bands, $cm^{-1}$): 2960 (w), 1478 (vs), 1362 (w), 1196 (m), 1107 (s), 972 (s), 908 (m), 871 (m), 800 (s), 732 (s).

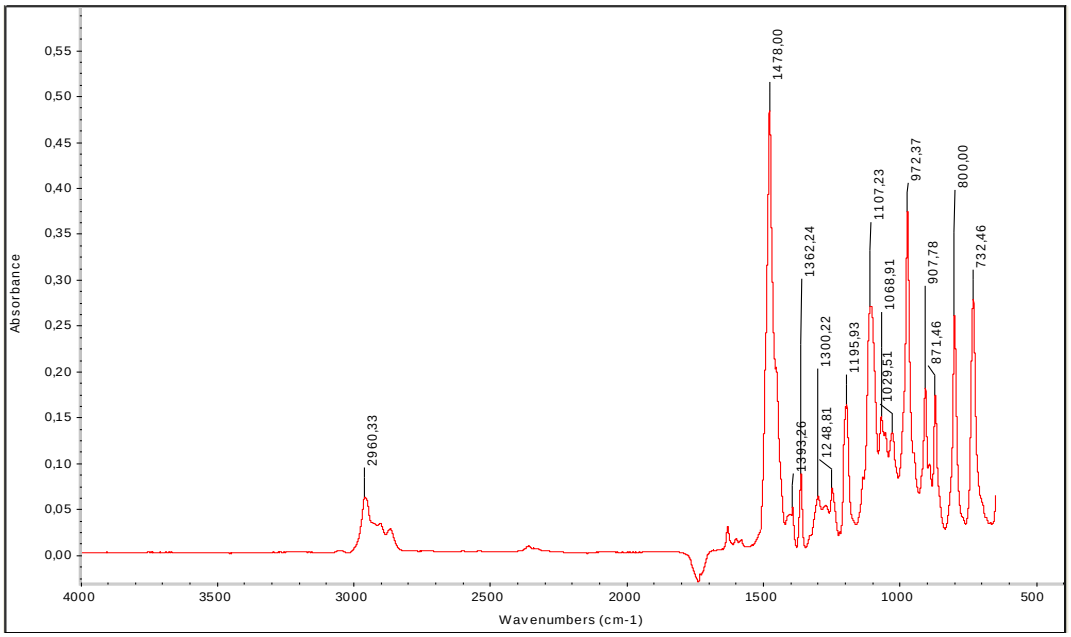



**Figure 1** FT-IR (UATR) of **B**.

***Synthesis of 1.$A_2$***: *C*-Pentyl-tetra(4-pyridyl)cavitand, **1** (0.020 g, 0.0178 mmol) was dissolved in 5mL of acetonitrile. To this solution was added 1,4-diiodo-tetrafluorobenzene, **A** (0.029 g, 0.0712 mmol) in 5 mL ethanol. The resulting solution was warmed and allowed to stand for slow evaporation at room temperature. Colorless, cubic crystals were obtained after 4 days. M.P.>300 °C; IR υ ($cm^{-1}$) 2925 (C-N stretch), 1603, 1460 (C-I stretch), 1216, 1086, 976, 942 (C-I bend), 584.

***Synthesis of 2.B***: *C*-Pentyl-tetra(3-pyridyl)cavitand, **2** (0.006 g, 0.0053 mmol) was dissolved in 5mL of ethanol. To this solution was added C-ethoxy-4-iodo-tetrafluorobenzene-tert-butylcalixarene, **B** (0.010 g, 0.0052 mmol) in 5 mL of ethanol. The resulting solution was warmed and allowed to stand for slow evaporation at room temperature. Colorless, rectangular crystals were obtained after 4 days. M. P. 185 - 187 °C; IR υ ($cm^{-1}$) 2928 (C-N stretch), 1727, 1480 (C-I stretch), 1241, 1106, 970, 948 (C-I bend), 583.

***Table 1 Crystallographic data for 1·$A_2$ and 2·B***

| | **1·$A_2$** | **2·B** |
|---|---|---|
| Empirical formula | C88 H82 F8 I4 N6 O8 | C150 H147 F16 I4 N5 O20.50 |
| Formula weight | 2011.20 | 3159.33 |
| Color | colorless cubic | colorless rectangular |
| Crystal size, $mm^3$ | 0.24 x 0.18 x 0.10 | 0.45 x 0.40 x 0.25 |
| Crystal system | Triclinic | Triclinic |
| Space group, Z | P-1, 2 | P-1, 2 |
| F(000) | 2000 | 3204 |
| a, Å | 12.3175(5) | 18.758(3) |
| b, Å | 13.2596(6) | 19.828(3) |
| c, Å | 25.4769(11) | 22.558(3) |
| α, ° | 88.893(2) | 100.106(10) |
| β, ° | 88.152(2) | 98.682(10) |
| γ, ° | 79.980(2) | 110.342(9) |
| volume, $Å^3$ | 4095.0(3) | 7538.1(19) |
| Density, $g/cm^3$ | 1.631 | 1.392 |
| Temperature, K | 120(2) | 120(2) |
| X-ray wavelength, Å | 0.71073 | 0.71073 |
| Absorption coefficient (μ), $mm^{-1}$ | 1.601 | 0.911 |
| θmin, ° | 0.80 | 1.13 |
| θmax, ° | 30.51 | 26.31 |
| Max. and min. transmission | 0.8563 and 0.7000 | 0.8043 and 0.6847 |
| Refinement method | Full-matrix least-squares on $F^2$ | Full-matrix least-squares on $F^2$ |
| Data / restraints / parameters | 22662 / 36 / 1057 | 32547 / 895 / 703 |
| Goodness-of-fit on $F^2$ | 1.033 | 2.282 |
| Reflections (collected) | 59351 | 32547 |
| (independent) | 22662 [R(int) = 0.0417] | 32547 [R(int) = 0.0000] |
| Final R indices [I>2sigma(I)] | R1 = 0.0513, wR2 = 0.1244 | R1 = 0.2143, wR2 = 0.4462 |
| R indices (all data) | R1 = 0.0806, wR2 = 0.1412 | R1 = 0.3441, wR2 = 0.4890 |
| Largest diff. peak and hole | 2.524 and -1.537 $e.Å^{-3}$ | 2.421 and -2.276 $e.Å^{-3}$ |

Datasets were collected on Bruker Kappa APEX II system at 120 K using APEX2 software.[(a)] An Oxford Croystream 700 low-temperature device was used to control temperature. MoK radiation was used. Initial cell constants were found by small widely separated "matrix" runs. Data collection strategies were determined using COSMO.[(b)] Scan speeds and scan widths were chosen based on scattering power and peak rocking curves.

Unit cell constants and orientation matrices were improved by least-squares refinement of reflections thresholded from the entire dataset. Integrations were performed with SAINT,[(c)] using these improved unit cells as a starting point. Precise unit cell constants were calculated in SAINT from the final merged datasets. Lorenz and polarization corrections were applied. Absorption corrections were applied as noted below.

Datasets were reduced with SHELXTL.[(d)] The structures were solved by direct methods without incident. All hydrogens were assigned to idealized positions and were allowed to ride. Isotropic thermal parameters for the hydrogen atoms were constrained to be 1.5x (methyl) / 1.2x (all other) that of the connected atom.

**1·A$_2$** The data were corrected for absorption with SADABS.[(d)] All non-hydrogen atoms were given anisotropic thermal parameters. For convenience the molecule was partitioned into four RESIdues (RESI 1 through RESI 4). Three of the four alkyl chains (on RESIdues 1, 2, and 3) were disordered and were split into two tails, with distance restraints applied throughout the alkyl chains with DFIX commands. Populations of the two alkyl chains in each disordered pair was controlled with free variables. Thermal parameters were constrained pairwise on the disordered fragments.

**2·B** (Fig. 1 and 2) The crystal was a non-merohedral twin and was processed with TWINABS. The contribution from each twin component was refined with a BASF variable. All atoms except for the iodines were handled with isotropic thermal parameters. The BUMP command was used to globally avoid close contacts. The asymmetric unit stoichiometry consists of: one pyridine-cavitand, one halobenzene-calixarene, one acetonitrile, and 4.5 waters.

***Solvent*** Because of the high thermal motion of water oxygens, as well as their distance from any obvious hydrogen-bond acceptor, hydrogen atoms were not located on the water molecules. Two waters (O1W and O2W) were refined with full occupancy, three water molecules (O3W, O4W and O5W) were refined with half occupancy, and one water molecule was refined as a disordered pair (O6A / O6B) with half occupancy each. An acetonitrile solvent molecule was located and refined successfully without any geometric restraints.

***Pyridine-cavitand*** For convenience the molecule was partitioned into four RESIdues (RESI 1 through RESI 4). Two of the four alkyl chains (on RESIdues 3 and 4) were disordered and were split into two tails, with distance restraints applied throughout the alkyl chains with DFIX commands. Populations of the two alkyl chains in each disordered pair was controlled with free variables. Thermal parameters were constrained pairwise on the disordered fragments. SIMU commands were used for each ordered alkyl chain in order to prevent excessive variation in

thermal parameters. Each pyridine ring was assigned a single thermal parameter with the EADP command. All benzene and pyridine rings were constrained to ideal benzene geometry with the AFIX 66 command.

***Halobenzene-calixarene*** For convenience the molecule was partitioned into four RESIdues (RESI 5 through RESI 8). Three of the four (aryloxy)ethyl side chains were fully ordered; the fourth (RESI 7) was disordered into three species. SIMU commands were used on each halobenzene group, and for each disordered oxyethylene bridge, in order to prevent excessive variation in thermal parameters. Each calixarene aryl ring was assigned a single thermal parameter with the EADP command, and each ethylene bridge was also assigned a single thermal parameter in the same manner. The haloarenes were restrained to planarity with FLAT commands. Geometries of all oxyethylene bridges were restrained to idealized geometry with DFIX and DANG commands.

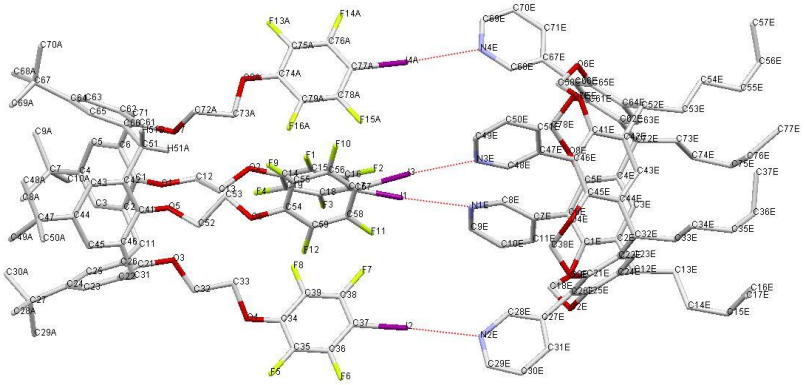


**Fig. 1** The closed dimeric capsule **2**(E)·**B**(A) with numbering scheme, stick style; only one of the conformers is reported, omitting H atoms, and solvated $CH_3CN$. The suffixes (E) and (A) are related to the different conformers (see the electronic supplementary information)..

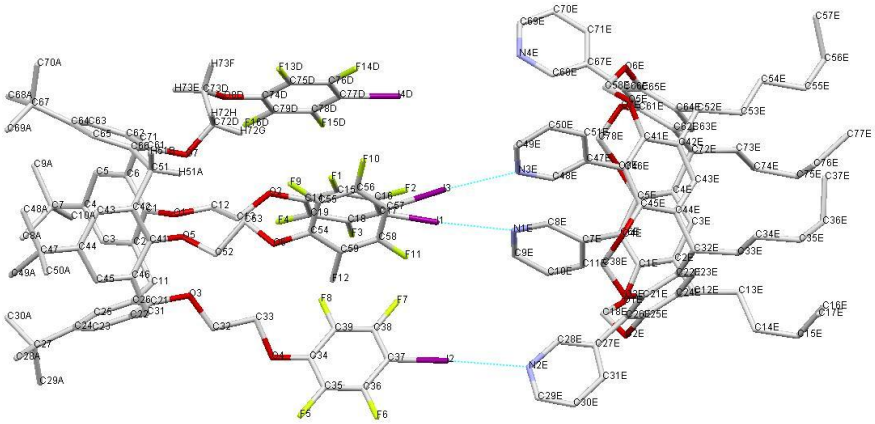


**Fig. 2** The opened dimeric capsule **2**(*E*)·**B**(*D*), drawn similarly to Figure 2. Here the distance N4E···I4D is about 5.18 Å, so that the cavitand may exchange the solvent with the outside.

(a) APEXII v2009. 5-1, © 2009, Bruker Analytical X-ray Systems, Madison, WI.

(b) COSMO v1. 60, © 1999 - 2009, Bruker Analytical X-ray Systems, Madison, WI.

(c) SAINT v7. 60a, © 1997 - 2008, Bruker Analytical X-ray Systems, Madison, WI.

(d) SHELXTL v2008/4, © 2008, , Bruker Analytical X-ray Systems, Madison, WI.

(e) SADABS v2008/1, © 2008, , Bruker Analytical X-ray Systems, Madison, WI.

(f) TWINABS v2008/4, © 2008, , Bruker Analytical X-ray Systems, Madison, WI.

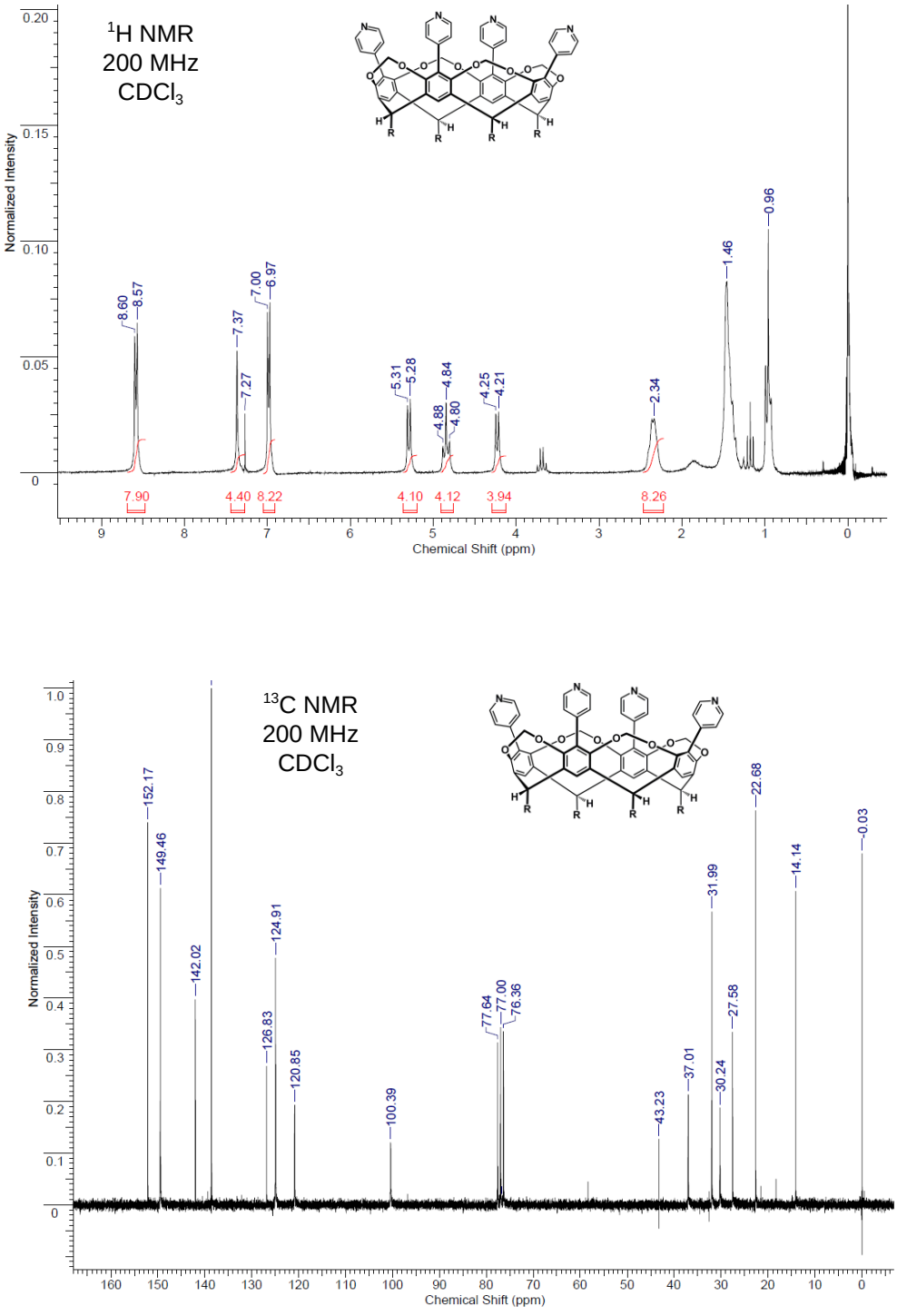



**Figure 2** $^{1}$H and $^{13}$C of *C*-Pentyltetra(4-pyridyl)cavitand, **1**.

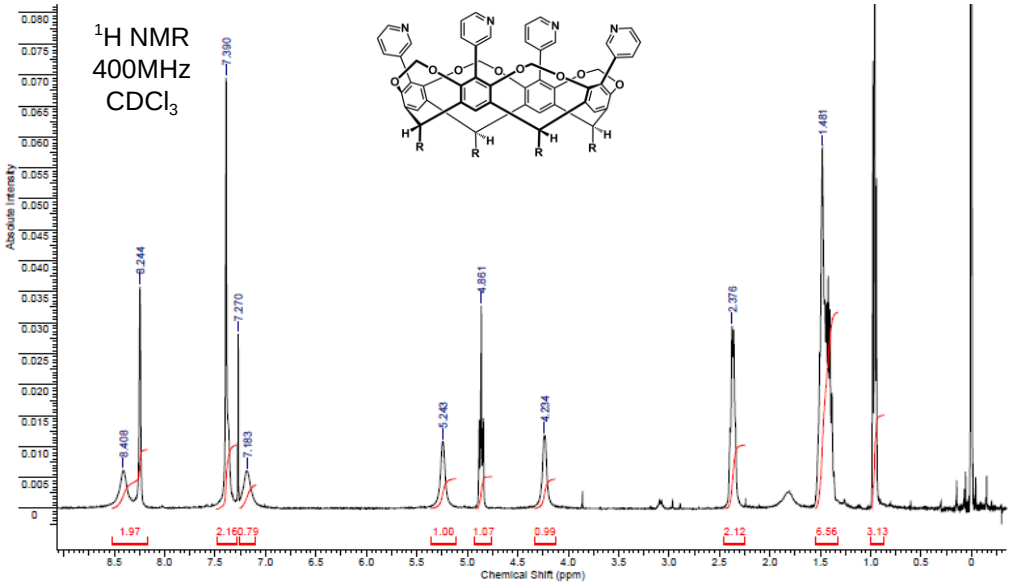



**Figure 3** $^1$H NMR of *C*-Pentyltetra(3-pyridyl)cavitand, **2**.

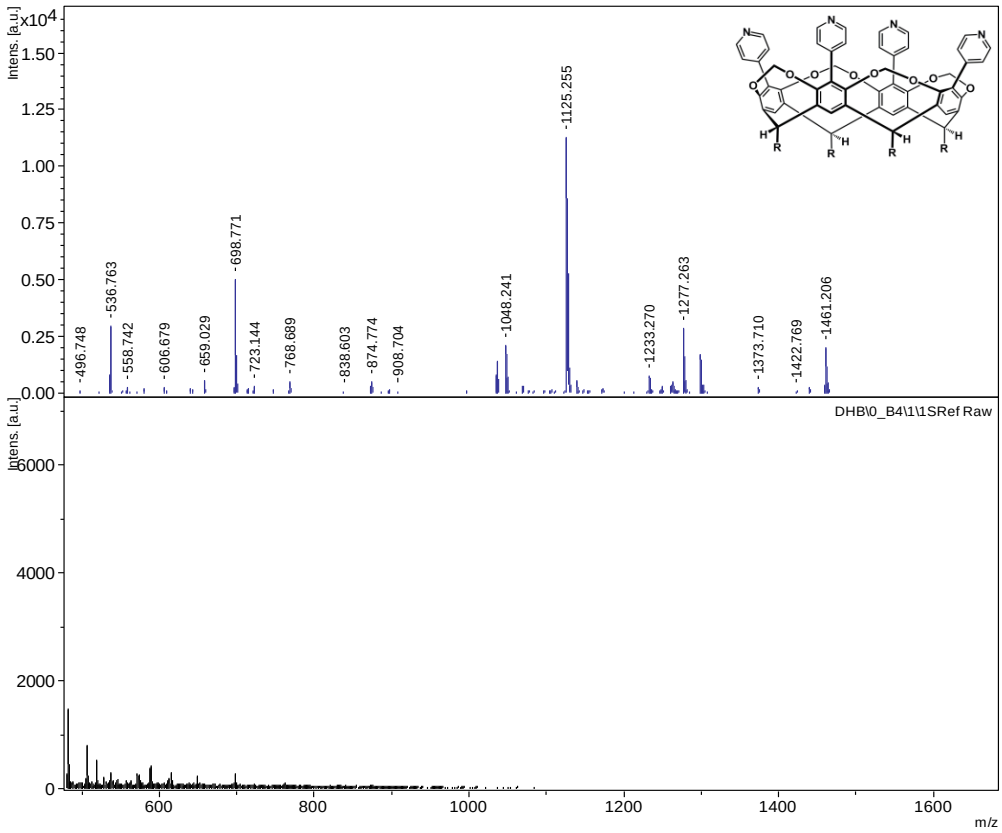



**Figure 4** Mass Spectra of *C*-Pentyltetra(4-pyridyl)cavitand, **1**.

[1] C.B. Aakeröy, N. Schultheiss, J. Desper, J. Org. Lett. 2006, **8**, 2607-2610

[2] Z. Asfari, A. Bilyk, C. Bond, J. M. Harrowfield, G. A. Koutsantonis, N. Lengkeek, M. Mocerino, B. W. Skelton, A. N. Sobolev, S. Strano, J. Vicens, A. H. White *Org. Biomol. Chem.*, 2004, **2**, 387–396.; P. L. H. M. Cobben, R. J. M. Egberink, J. G. Bomer, R. Bergveld, W. Verboom, D. N. Reinhoudt *J. Am. Chem. Soc.* 1992, **114**, 10573-10582.